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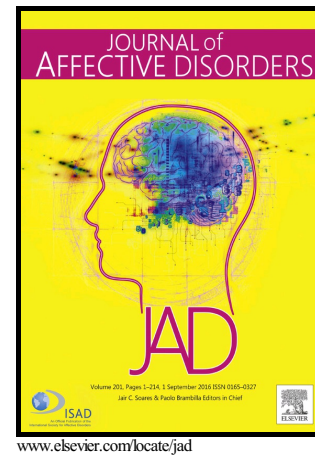
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Relationship between sedentary behavior and depression: a mediation analysis of influential factors across the lifespan among 42,469 people in low- and middle-income countries

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Relationship between sedentary behavior and depression: a mediation analysis of influential factors across the lifespan among 42,469 people in low- and middle-income countries

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Abstract

Background

Sedentary behavior (SB) is associated with diabetes, cardiovascular disease and low mood. There is a paucity of multi-national research investigating SB and depression, particularly among low- and middle-income countries. This study investigated the association between SB and depression, and factors which influence this.

Methods

Cross-sectional data were analyzed from the World Health Organization's Study on Global Ageing and Adult Health. Depression was based on the Composite International Diagnostic Interview. The

association between depression and SB (self-report) was estimated by multivariable linear and logistic regression analyses. Mediation analysis was used to identify influential factors.

Results

A total of 42,469 individuals (50.1% female, mean 43.8 years) were included. People with depression spent 25.6 (95%CI 8.5-42.7) more daily minutes in SB than non-depressed participants. This discrepancy was most notable in adults aged ≥ 65 y (35.6 minutes in those with depression). Overall, adjusting for socio-demographics and country, depression was associated with a 1.94 (95%CI 1.31-2.85) times higher odds for high SB (i.e., ≥ 8 h/day). The largest proportion of the SB-depression relationship was explained by mobility limitations (49.9%), followed by impairments in sleep/energy (43.4%), pain/discomfort (31.1%), anxiety (30.0%), disability (25.6%), cognition (16.1%), and problems with vision (11.0%). Other health behaviors (physical activity, alcohol consumption, smoking), body mass index, and social cohesion did not influence the SB-depression relationship.

Conclusion

People with depression are at increased risk of engaging in high levels of SB. This first multi-national study offers potentially valuable insight for a number of hypotheses which may influence this relationship, although testing with longitudinal studies is needed.

Keywords: sedentary behavior, sitting, physical activity, depression, low- and middle-income countries

Introduction

Depression is a leading cause of global years lived with disability (Whiteford, Ferrari et al. 2015). Whilst depression is associated with elevated mortality due to suicide (Hawton, Casanas et al. 2013), cardio-metabolic diseases are the leading cause of premature death (Correll, Solmi et al. 2017). It is known that people with depression have a double increased risk for diabetes and cardiovascular diseases compared to the general population (Vancampfort, Stubbs et al. 2015, Vancampfort, Correll et al. 2016, Stubbs, Vancampfort et al. 2017).

There is established evidence that physical activity (PA) is good for health and confers comparable benefits to pharmacological interventions for preventing cardiovascular mortality (Naci and Ioannidis

2013). People with established depression are known to engage in low levels of moderate-vigorous PA and are less likely than age-sex matched controls to meet recommended PA guidelines (Schuch, Vancampfort et al. 2016). Recent research has demonstrated that low levels of physical activity (PA) are consistently associated with an elevated risk for depression (Mammen and Faulkner 2013, Stubbs, Koyanagi et al. 2016). Furthermore, engaging in structured physical activity ("exercise") has been demonstrated to be an effective treatment for depression (Schuch, Vancampfort et al. 2016).

There is also increasing evidence in the general population demonstrating that sedentary behavior (SB) is associated with a range of deleterious outcomes such as diabetes, cancer, cardiovascular disease and associated premature mortality (Biswas, Oh et al. 2015). SB refers to any waking behavior characterized by an energy expenditure ≤ 1.5 metabolic equivalents (METs), while in a sitting, reclining or lying posture (Sedentary Behaviour Research 2012, Tremblay, Aubert et al. 2017). Much like depression, SB is highly prevalent and pervasive in societies across the world (Bennie, Chau et al. 2013, Ekelund, Steene-Johannessen et al. 2016, Løyen, Verloigne et al. 2016). Within the past five years, there has been growing interest in the potential relationship between SB and depression. A recent meta-analysis, almost exclusively among high-income countries, found that among 110,152 individuals, higher levels of SB were associated with depression (relative risk 1.31 (95%CI 1.16 to 1.48)) (Zhai, Zhang et al. 2015). Whilst recent advances in the literature have shone light on this neglected issue, a number of biases and gaps exist in the literature exploring the relationship between SB and depression to date. First, there is a paucity of multinational studies exploring the association between depression and SB. The current focus of micro-populations within specific countries may have limited utility beyond their immediate setting. Second, there is notably limited data on this association in low- and middle-income countries (LMICs), despite the increasing rates of non-communicable diseases and sedentary lifestyles (Christensen, Doblhammer et al. 2009) in LMICs. Exploring associations between depression and SB in LMICs is also important given the high levels of depression (Guerra, Prina et al. 2016) and the low levels of knowledge regarding the risks associated with SB in LMICs (Pengpid, Peltzer et al. 2015), and compared with HICs, different occupational and socio-cultural structures, methods of transportation, and environmental factors (e.g., safety, climate) (Atkinson, Lowe et al. 2016). The continuing dearth of studies from LMICs also highlights the gap between where research is conducted and where the largest public health impacts of physical

inactivity (defined as not meeting recommended physical activity guidelines) occur (Sallis, Bull et al. 2016). Third, many studies investigating the association between SB and depression have relied upon screening tools such as the Patient Health Questionnaire (Adamson, Yang et al. 2016), which have limited sensitivity and specificity for identifying “true” depression (Mitchell, Yadegarfar et al. 2016). Finally, despite the association between depression and SB reported in previous high-income populations, a paucity of research has considered what variables might influence the relationship. Clearly, understanding the influential factors in this relationship, such as sociodemographic (e.g. age, sex, employment status), mental/physical health (e.g. physical comorbidities) and health behaviors (e.g. smoking, alcohol use, mobility), may prove useful for developing effective interventions in the future.

The current study used a large, multi-national sample and sought to investigate (1) the association between depression and SB across 6 LMICs; and (2) to investigate the factors that may explain the relation between depression and SB.

Methods

The survey

Data from the Study on Global Ageing and Adult Health (SAGE) survey was analyzed. The survey was conducted between 2007 and 2010 in China, Ghana, India, Mexico, Russia, and South Africa, which were all LMICs at the time of the survey according to the World Bank classification. Details of the survey methodology are provided elsewhere (Kowal, Chatterji et al. 2012). Briefly, in order to obtain nationally representative samples, a multi-stage clustered sampling design method was used. The sample consisted of adults aged ≥ 18 years with oversampling of those aged ≥ 50 years. Trained interviewers conducted face-to-face interviews using a standard questionnaire across countries to collect information. Standard translation procedures for the questionnaires were undertaken to ensure comparability between countries. Sampling weights were calculated to adjust for the population structure as reported by the United Nations Statistical Division. Ethical approval was obtained from the WHO Ethical Review Committee and local ethics research review boards. Written informed consent was obtained from all participants. The survey response rate ranged from 51% (Mexico) to 93% (China). Full details of the sampling strategy are displayed in supplementary file 1.

Variables

Sedentary behaviour (Outcome variable)

In order to assess SB, participants were asked to state the total time they usually spent (expressed in minutes per day) sitting or reclining including at work, at home, getting to and from places, or with friends (e.g., sitting at a desk, sitting with friends, travelling in car, bus, train, reading, playing cards or watching television). This did not include time spent sleeping. The variable on SB was used in the analysis as a continuous variable (minutes per day) and also as a categorical [<8 or ≥ 8 hours per day (high SB)] variable in line with recent publications (Vancampfort, Koyanagi et al. 2017, Vancampfort, Stubbs et al. 2017). The eight-hour cut-off was chosen as previous research indicated that being sedentary for ≥ 8 hours/day in the general population is associated with a higher risk for premature mortality (Ekelund, Steene-Johannessen et al. 2016).

Depression (Exposure variable)

Questions based on the World Mental Health Survey version of the Composite International Diagnostic Interview (Kessler and Ustun 2004) were used for the endorsement of past 12-month DSM-IV depression using the same algorithm used in previous studies using the same dataset (Koyanagi, Garin et al. 2014, Garin, Koyanagi et al. 2016) (Details provided in **eTable 1**).

*Potential mediators**Health status:*

was evaluated with 10 health-related questions pertaining to five health domains including: (a) mobility; (b) pain and discomfort; (c) cognition; (d) vision; (e) sleep and energy. Each of the five domains corresponds to those in common health related quality of life outcome measures such as the Short Form-12 (SF-12) (Ware, Kosinski et al. 1996), the Health Utilities Index Mark-3 (HUI) (Feeny, Furlong et al. 1995) and the EUROQOL-5D (Kind 1996). Each domain consists of two questions that assessed health function in the past 30 days. The actual questions can be found in supplementary **eTable 2**. Each item was scored on a five-point scale ranging from 'none' to 'extreme/cannot do'. For each separate domain, we used factor analysis with polychoric correlations to obtain a factor score which was later converted to scores ranging from 0-100 with higher values representing worse health function (Stubbs, Koyanagi et al. 2016, Stubbs, Koyanagi et al. 2016).

Anxiety:

In accordance with previous publications using a dataset with the identical question, those who claimed to have severe/extreme problems with worry or anxiety in the past 30 days were considered to have anxiety (Stubbs, Koyanagi et al. 2017, Vancampfort, Koyanagi et al. 2017).

Disability:

was assessed with six questions on the level of difficulty in conducting standard basic activities of daily living (ADL) in the past 30 days (washing whole body, getting dressed, moving around inside home, eating, getting up from lying down, and using the toilet) (Katz, Ford et al. 1963). Those who answered severe or extreme/cannot do to any of the six questions were considered to have disability (Koyanagi, Moneta et al. 2015).

Physical activity:

Levels of physical activity was assessed with the Global Physical Activity Questionnaire (Bull, Maslin et al. 2009). The total amount (min) of moderate-to-vigorous physical activity in a typical week was calculated.

Alcohol consumption and smoking:

referred to current smoking (Y/N) and alcohol use in the past 30 days (Y/N) respectively.

Body mass index (BMI):

A stadiometer and a routinely calibrated electronic weighting scale were used to measure height and weight respectively. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared, and categorized as <18.5 (underweight), 18.5-24.9 (normal), 25.0-29.9 (overweight), and ≥ 30 (obese) kg/m^2 .

Social cohesion:

In accordance with a previous SAGE publication (Zamora-Macorra, de Castro et al. 2017), a social cohesion index was created based on nine questions on the participant's involvement in community activities in the past 12 months (e.g., attended religious services, club, society, union etc) with answer options 'never (coded=0)', 'once or twice per year (coded=1)', 'once or twice per month (coded=2)', 'once or twice per week (coded=3)', and 'daily (coded=4)'. The answers to these questions were summed (range 0-36) with higher scores indicating higher levels of social cohesion.

Control variables

These included sociodemographic variables such as sex, age, wealth, highest level of education achieved (\leq primary, secondary, \geq tertiary), marital status (married/cohabiting or never married/separated/divorced/widowed), setting (urban or rural), and employment status (engaged in paid work ≥ 2 days in last 7 days: Y/N). Wealth quintiles were created based on country-specific income. These variables were not considered as potential mediators as sociodemographic variables are generally considered to be non-modifiable.

Statistical analysis

The statistical analysis was done with Stata 14.1 (Stata Corp LP, College station, Texas). The difference in sample characteristics between those with and without depression or high SB was tested by Student's *t*-tests and Chi-squared tests for continuous and categorical variables, respectively. Multivariable logistic and linear regression analyses were used to assess the association between depression (exposure) and SB (outcome). The main analysis consisted of the logistic regression analysis using the binary SB variable (i.e., < 8 or ≥ 8 hours/day) as the outcome. This analysis was intended to assess the specific association between depression and high levels of SB. A secondary analysis using linear regression with the continuous variable (min/day of SB) as the outcome was also conducted to assess increasing or decreasing levels of SB associated with depression. A base model was constructed adjusting for the sociodemographic variables (i.e., sex, age, wealth, education, marital status, setting, employment status), and country.

Next, in order to gain an understanding of the extent to which various factors may explain the relation between depression and high SB, we conducted mediation analysis. Specifically, we focused on mobility, pain and discomfort, cognition, sleep and energy, vision, anxiety, and disability, physical activity, alcohol consumption, smoking, BMI, and social cohesion for their previously reported association with the exposure (depression) and the outcome (high SB) (Stubbs, Patchay et al. 2014, Biswas, Oh et al. 2015, O'Donoghue, Perchoux et al. 2016, Lakerveld, Luyen et al. 2017, Prince, Reed et al. 2017, Wirth, Klenk et al. 2017). We used the *kmb* (Karlson Holm Breen) command in Stata (Breen, Karlson et al. 2013) for this purpose. This method can be applied in logistic regression models and decomposes the total effect (i.e., unadjusted for the mediator) of a variable into direct (i.e., the effect of depression on SB adjusted for the mediator) and indirect effects (i.e., the mediational effect). Using this method, the percentage of the main association explained by the mediator can also be

calculated (mediated percentage). Each potential mediator was included in the model individually. The mediation analysis controlled for the sociodemographic variables and country.

For the regression analyses, we conducted analysis using the overall sample and by age groups (age 18-49, 50-64, ≥ 65 years). All regression analyses were adjusted for country by including dummy variables for each country. All variables were included in the models as categorical variables with the exception of the variable on age, min/day of SB, social cohesion, health status (mobility, pain and discomfort, cognition, sleep and energy, vision), and physical activity (continuous variables). Under 3% of the data were missing for the variables used in the current analysis with the exception of BMI (5.8%). Complete case analysis was done. The sample weighting and the complex study design were taken into account in all analyses. Results from the regression analyses are presented as odds ratios (ORs) or b-coefficients with 95% confidence intervals (CIs). The level of statistical significance was set at $P < 0.05$.

Results

A total of 42,469 (China $n=14,811$; Ghana $n=5108$; India $n=11,230$; Mexico $n=2742$; Russia $n=4355$; South Africa $n=4223$) individuals (50.1% female) with a mean (SD) age of 43.8 (14.4) years were included in the analysis. The overall prevalence (95%CI) of high SB (i.e., ≥ 8 h/day of SB) was 8.3% (7.1%-9.7%), while the mean (SD) minutes/day spent sedentary across the whole sample was 207 (149). The overall prevalence (95%CI) of depression was 4.1% (3.6%-4.6%). The prevalence of depression was particularly high among those with ≥ 8 h hours/day of SB, with 9.3% of those spending ≥ 11 hours/day sedentary having depression (see **Figure 1**). The sample characteristics are provided in **Table 1**. Factors such as older age, not being married/cohabiting, unemployment, mobility limitations, sleep/energy disruption, and disability were strongly associated with both depression and high SB.

In models adjusted for sociodemographics and country, depression was associated with a 1.94 (95%CI=1.31-2.85) times higher odds for high SB, while the mean time spent sedentary was 26 (95%CI=9-43) minutes longer per day among depressed individuals (**Table 2**). Estimates across age groups were similar. The results of the mediation analysis that assessed the degree to which the

association between depression and high SB can be explained by various factors are illustrated in **Table 3** and **4**. Based on the overall sample, the largest proportion of the total effect was explained by mobility limitations (49.9%), followed by impairments in sleep/energy (43.4%), pain/discomfort (31.1%), anxiety (30.0%), disability (25.6%), cognition (16.1%), and problems with vision (11.0%) (Table 3). Mobility and pain/discomfort explained more than 50% of the association in individuals aged ≥ 65 years. Cognition and anxiety were important mediators mainly among older adults. Health behaviors (physical activity, alcohol consumption, smoking), BMI, and social cohesions were not significant mediators (i.e., no significant indirect effects) in the overall sample or any of the age groups

Discussion

To the best of our knowledge, ours is the first multi-national study to investigate the relationship between depression and SB and its influential factors. Our data suggest that higher levels of SB (particularly over 11 hours) are associated with an elevated prevalence of depression. The relationship between high levels of SB and depression held across the lifespan, and depression across the entire sample was associated with a 26-minute increase in SB per day. Previous research has found that such differences in SB are associated with worse cardiometabolic health (Katzmarzyk 2010, Katzmarzyk and Lee 2012), increased inflammation and worse mood profile (Endrighi, Steptoe et al. 2015). Interestingly, we found evidence that mobility limitations, disability and sleep problems explained the relationship between depression and SB across all age ranges. Moreover, smoking, alcohol consumption, BMI, physical activity and social cohesion had little influence in the association between depression and SB. Given the high levels of SB among those with depression previously reported (Schuch, Vancampfort et al. 2016), and the deleterious outcomes of high levels of SB in the general population (Biswas, Oh et al. 2015), our data provide important insights that might help shape future interventions.

In addition to extending the literature on being the first multinational study to explore the association between depression and SB, our study provides some indication of factors that may influence this relationship. Perhaps unsurprisingly, we found evidence across all age groups that mobility limitations mediated 49% of the association between SB and depression. Mobility limitations can arise from a multitude of problems, and have previously been associated with SB (Stubbs, Patchay et al. 2014)

and an increased risk of developing depression (Veronese, Stubbs et al. 2017). Importantly, increasing PA among people with mobility limitations can reduce the risk of developing activities of daily living difficulties (Tak, Kuiper et al. 2013) and promote healthy ageing (Daskalopoulou, Stubbs et al. 2017). When one considers that low PA is associated with depression (Mammen and Faulkner 2013) and depression reduces with participation in PA (Schuch, Vancampfort et al. 2016), strategies to designed as sitting reduction interventions tailored to those with mobility limitations may play a pivotal role in this population. We also observed that pain, particularly among older adults explained a considerable proportion of the association between SB and depression. Pain is known to be highly comorbid with depression (Stubbs, Koyanagi et al. 2016, Stubbs, Vancampfort et al. 2017), particularly among older adults (Abdulla, Bone et al. 2013) and is associated with low PA (Stubbs, Binnekade et al. 2013) and SB (Stubbs, Patchay et al. 2014). Interestingly, we also found a relationship between sleep and energy problems as an important influential factor across all age ranges. Sleep and energy issues are known to be a core feature of depression and are closely linked to energy expenditure (Luca, Luca et al. 2013). Prolonged periods of SB are known to increase tiredness and predispose people to “napping” which has been associated with depression (Luca, Luca et al. 2013) and other deleterious outcomes such as a poor cardio-metabolic profile (Yamada, Hara et al. 2015). Future interventions that address sleep and in particular daytime napping may play an important role in preventing high levels of SB and depression.

Whilst in the overall sample, anxiety mediated 30% of the association between SB and depression, this relationship was only evident in working and older age adults. Depression and anxiety are often comorbid (Rebar, Stanton et al. 2017) and anxiety has been associated with SB (Teychenne, Costigan et al. 2015). Whilst PA can reduce anxiety symptoms (Stubbs, Vancampfort et al. 2017), our data suggest that PA does not per se influence the SB and depression relationship. Whilst our data cannot provide a causal inference, some previous studies can provide some indication of a potentially causal relationship which underpin our assertions. For instance, previous research from randomized controlled trials in Western samples has demonstrated the independent deleterious impact of increasing SB on mood and in particular symptoms of anxiety (Edwards and Loprinzi 2016), possibly through changes in inflammation (Endrighi, Steptoe et al. 2015). Previous research has also suggested that SB is also associated with inflammation, most notably c-reactive protein and

interleukin 6 (Henson, Yates et al. 2013, Wirth, Klenk et al. 2017). There is some provisional evidence to suggest that standing and breaking up prolonged periods of SB can improve inflammatory biomarkers profiles (Healy, Dunstan et al. 2008, Owen, Healy et al. 2010, Healy, Matthews et al. 2011, Hansen, Wijndaele et al. 2012). Thus, future interventions may consider investigating the potential benefits of disrupting SB on mood (depression and anxiety) and underlying mechanisms of potential change, such as inflammation. We also found some evidence that cognition influenced SB and depression, notably among working and older age adults. There is evidence that both depression (Rock, Roiser et al. 2014) and SB (Falck, Davis et al. 2016) are associated with cognitive impairment. Whether or not reducing SB can improve cognition is unclear, although there is robust evidence that PA can improve cognition (Stanmore, Stubbs et al. 2017), however, this did not appear to influence the SB and depression relationship in our data.

Surprisingly, none of the measured health behaviors (alcohol use, PA, smoking), or risk factors (body mass index, social cohesion) influenced the SB-depression relationship. Many of these findings are inconsistent with the wider literature. For example, PA has been shown to have a multitude of benefits for both depression and many of the other potential influencing factors (e.g. disability, mobility, cognition), and so could be expected to influence the impact of SB on depression. Similarly, BMI is known to be associated with SB (Wirth, Klenk et al. 2017) and depression (Vancampfort, Stubbs et al. 2015, Vancampfort, Correll et al. 2016, Fornaro, Solmi et al. 2017). However, simply being correlated with both SB and depression does not mean that BMI is a potential mediator of this relationship and clearly, future longitudinal research is required to disentangle the relationships we observed and explore potentially modifiable mediators. Future research is also required to consider the type and context of SB (e.g. sitting at home, work) and depression, preferably using a longitudinal design and objective measures of SB.

The current findings should be interpreted in light of some limitations. First, the study is cross-sectional, therefore the directionality of the relationships cannot be deduced with certainty. The aim of the study was only to quantify the degree to which potentially influential factors in the depression-SB relationship may explain this association. Thus, directionality or causality cannot be established and the effect of these influential factors as mediators or confounders cannot be known. Therefore, future

longitudinal studies are required to better disentangle the relationships we observed. Second, SB was captured with a self-report measure, the accuracy of which has been questioned (Soundy, Roskell et al. 2014, Stubbs, Firth et al. 2016). Future research should utilize objective measures of SB. Accelerometers-inclinometers are available that allow for valid and reliable objective measures of SB (Grant et al, 2006). Finally, we have not investigated context specific SB (e.g. TV viewing) which may provide important insights into the underlying relationships we observed. Nonetheless, the strengths of the study include the large sample size (over 42,000) and the multi-national scope. Most of the research in the domain of SB and depression has been conducted in Western countries, and little is known about these experiences and mediators in regions across which there are multiple economic, cultural or social factors or differences in the health systems. The present study was furthermore performed with nationally representative samples of non-institutionalized persons. Moreover, by conducting mediation analyses, we have advanced the understanding of factors influencing SB and depression, which has largely been missing from the literature to date.

In conclusion, our paper provides evidence of a relationship between SB and depression. In fact, across this representative cohort over 6 countries, being depressed was associated with 26 more daily minutes of sedentary time. Mobility limitations, pain and discomfort, cognition problems, sleep and energy issues, anxiety and disability may potentially influence the relationship between SB and depression. If replicated using longitudinal designs to more reliably establish directionality/causality, these findings could offer important new targets and strategies for interventions to tackle the depression-SB relationship.

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None

AUTHOR STATEMENT DOCUMENT

Contributors

BS, DV, AK devised the study and conducted and oversaw the analyses and wrote the manuscript. All authors provided critical comments and approved the final manuscript.

Conflict of interest

None to declare from any author

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References

- Abdulla, A., M. Bone, N. Adams, A. M. Elliott, D. Jones, R. Knaggs, D. Martin, E. L. Sampson and P. Schofield (2013). Evidence-based clinical practice guidelines on management of pain in older people. *Age & Ageing*. **42**: 151-153.
- Adamson, B. C., Y. Yang and R. W. Motl (2016). "Association between compliance with physical activity guidelines, sedentary behavior and depressive symptoms." *Prev Med* **91**: 152-157.
- Atkinson, K., S. Lowe and S. Moore (2016). "Human development, occupational structure and physical inactivity among 47 low and middle income countries." *Prev Med Rep* **3**: 40-45.
- Bennie, J. A., J. Y. Chau, H. P. van der Ploeg, E. Stamatakis, A. Do and A. Bauman (2013). "The prevalence and correlates of sitting in European adults - a comparison of 32 Eurobarometer-participating countries." *Int J Behav Nutr Phys Act* **10**: 107.
- Biswas, A., P. I. Oh, G. E. Faulkner, R. R. Bajaj, M. A. Silver, M. S. Mitchell and D. A. Alter (2015). "Sedentary Time and Its Association With Risk for Disease Incidence, Mortality, and Hospitalization in Adults: A Systematic Review and Meta-analysis." *Annals of Internal Medicine* **162**(2): 123-132.
- Breen, R., K. B. Karlson and A. Holm (2013). "Total, Direct, and Indirect Effects in Logit and Probit Models." *Sociological Methods & Research* **42**(2): 164-191.
- Bull, F. C., T. S. Maslin and T. Armstrong (2009). "Global physical activity questionnaire (GPAQ): nine country reliability and validity study." *J Phys Act Health* **6**(6): 790-804.
- Christensen, K., G. Doblhammer, R. Rau and J. W. Vaupel (2009). "Ageing populations: the challenges ahead." *Lancet* **374**(9696): 1196-1208.
- Correll, C. U., M. Solmi, N. Veronese, B. Bortolato, S. Rosson, P. Santonastaso, N. Thapa-Chhetri, M. Fornaro, D. Gallicchio, E. Collantoni, G. Pigato, A. Favaro, F. Monaco, C. Kohler, D. Vancampfort, P. B. Ward, F. Gaughran, A. F. Carvalho and B. Stubbs (2017). "Prevalence, incidence and mortality from cardiovascular disease in patients with pooled and specific severe mental illness: a large-scale meta-analysis of 3,211,768 patients and 113,383,368 controls." *World Psychiatry* **16**(2): 163-180.
- Daskalopoulou, C., B. Stubbs, C. Kralj, A. Koukounari, M. Prince and A. M. Prina (2017). "Physical Activity and Healthy Ageing: A Systematic Review and Meta-analysis of longitudinal cohort studies." *Ageing Res Rev*.
- Edwards, M. K. and P. D. Loprinzi (2016). "Experimentally increasing sedentary behavior results in increased anxiety in an active young adult population." *J Affect Disord* **204**: 166-173.

- Ekelund, U., J. Steene-Johannessen, W. J. Brown, M. W. Fagerland, N. Owen, K. E. Powell, A. Bauman, I.-M. Lee, L. P. A. Series and L. S. B. W. Group (2016). "Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women." *The Lancet* **388**(10051): 1302-1310.
- Ekelund, U., J. Steene-Johannessen, W. J. Brown, M. W. Fagerland, N. Owen, K. E. Powell, A. Bauman and I. M. Lee (2016). "Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women." *Lancet* **388**(10051): 1302-1310.
- Endrighi, R., A. Steptoe and M. Hamer (2015). "The effect of experimentally induced sedentariness on mood and psychobiological responses to mental stress." *The British Journal Of Psychiatry: The Journal Of Mental Science*.
- Falck, R. S., J. C. Davis and T. Liu-Ambrose (2016). "What is the association between sedentary behaviour and cognitive function? A systematic review." *Br J Sports Med*.
- Feeny, D., W. Furlong, M. Boyle and G. W. Torrance (1995). "Multi-attribute health status classification systems. Health Utilities Index." *Pharmacoeconomics* **7**(6): 490-502.
- Fornaro, M., M. Solmi, N. Veronese, D. De Berardis, E. F. Buonaguro, C. Tomasetti, G. Perna, A. Preti and M. G. Carta (2017). "The burden of mood-disorder/cerebrovascular disease comorbidity: essential neurobiology, psychopharmacology, and physical activity interventions." *Int Rev Psychiatry* **29**(5): 425-435.
- Garin, N., A. Koyanagi, S. Chatterji, S. Tyrovolas, B. Olaya, M. Leonardi, E. Lara, S. Koskinen, B. Tobiasz-Adamczyk, J. L. Ayuso-Mateos and J. M. Haro (2016). "Global Multimorbidity Patterns: A Cross-Sectional, Population-Based, Multi-Country Study." *J Gerontol A Biol Sci Med Sci* **71**(2): 205-214.
- Guerra, M., A. M. Prina, C. P. Ferri, D. Acosta, S. Gallardo, Y. Huang, K. S. Jacob, I. Z. Jimenez-Velazquez, J. J. Llibre Rodriguez, Z. Liu, A. Salas, A. L. Sosa, J. D. Williams, R. Uwakwe and M. Prince (2016). "A comparative cross-cultural study of the prevalence of late life depression in low and middle income countries." *J Affect Disord* **190**: 362-368.
- Hansen, A. L. S., K. Wijndaele, N. Owen, D. J. Magliano, A. A. Thorp, J. E. Shaw and D. W. Dunstan (2012). "Adverse associations of increases in television viewing time with 5-year changes in glucose homeostasis markers: the AusDiab study." *Diabetic Medicine* **29**(7): 918-925.
- Hawton, K., I. C. C. Casanas, C. Haw and K. Saunders (2013). "Risk factors for suicide in individuals with depression: a systematic review." *J Affect Disord* **147**(1-3): 17-28.
- Healy, G. N., D. W. Dunstan, J. Salmon, E. Cerin, J. E. Shaw, P. Z. Zimmet and N. Owen (2008). "Breaks in Sedentary Time." *Diabetes Care* **31**(4): 661-666.
- Healy, G. N., C. E. Matthews, D. W. Dunstan, E. A. H. Winkler and N. Owen (2011). "Sedentary time and cardio-metabolic biomarkers in US adults: NHANES 2003-06." *European Heart Journal* **32**(5): 590-597.
- Henson, J., T. Yates, C. L. Edwardson, K. Khunti, D. Talbot, L. J. Gray, T. M. Leigh, P. Carter and M. J. Davies (2013). "Sedentary Time and Markers of Chronic Low-Grade Inflammation in a High Risk Population." *PLoS ONE* **8**(10): 1-6.
- Katz, S., A. B. Ford, R. W. Moskowitz, B. A. Jackson and M. W. Jaffe (1963). "Studies of illness in the aged. The index of ADL: A standardized measure of biological and psychosocial function." *Jama* **185**: 914-919.
- Katzmarzyk, P. T. (2010). "Physical activity, sedentary behavior, and health: paradigm paralysis or paradigm shift?" *Diabetes* **59**(11): 2717-2725.
- Katzmarzyk, P. T. and I. M. Lee (2012). "Sedentary behaviour and life expectancy in the USA: a cause-deleted life table analysis." *BMJ Open* **2**(4).
- Kessler, R. C. and T. B. Ustun (2004). "The World Mental Health (WMH) Survey Initiative Version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI)." *Int J Methods Psychiatr Res* **13**(2): 93-121.

- Kind, P. (1996). The Euroqol instrument: an index of health-related quality of life. *Quality of Life and Pharmacoeconomics in Clinical Trial*. B. Spiker, Lippincott-Raven Publishers: 191-201.
- Kowal, P., S. Chatterji, N. Naidoo, R. Biritwum, W. Fan, R. Lopez Ridaura, T. Maximova, P. Arokiasamy, N. Phaswana-Mafuya, S. Williams, J. J. Snodgrass, N. Minicuci, C. D'Este, K. Peltzer and J. T. Boerma (2012). "Data resource profile: the World Health Organization Study on global AGEing and adult health (SAGE)." *Int J Epidemiol* **41**(6): 1639-1649.
- Koyanagi, A., N. Garin, B. Olaya, J. L. Ayuso-Mateos, S. Chatterji, M. Leonardi, S. Koskinen, B. Tobiasz-Adamczyk and J. M. Haro (2014). "Chronic conditions and sleep problems among adults aged 50 years or over in nine countries: a multi-country study." *PLoS One* **9**(12): e114742.
- Koyanagi, A., M. V. Moneta, N. Garin, B. Olaya, J. L. Ayuso-Mateos, S. Chatterji, M. Leonardi, P. Sainio, A. Galas and J. M. Haro (2015). "The association between obesity and severe disability among adults aged 50 or over in nine high-income, middle-income and low-income countries: a cross-sectional study." *BMJ Open* **5**(4): e007313.
- Lakerveld, J., A. Luyen, N. Schotman, C. F. W. Peeters, G. Cardon, H. P. van der Ploeg, N. Lien, S. Chastin and J. Brug (2017). "Sitting too much: A hierarchy of socio-demographic correlates." *Prev Med* **101**: 77-83.
- Luyen, A., M. Verloigne, L. Van Hecke, I. Hendriksen, J. Lakerveld, J. Steene-Johannessen, A. Koster, A. Donnelly, U. Ekelund, B. Deforche, I. De Bourdeaudhuij, J. Brug and H. P. van der Ploeg (2016). "Variation in population levels of sedentary time in European adults according to cross-European studies: a systematic literature review within DEDIPAC." *Int J Behav Nutr Phys Act* **13**: 71.
- Luca, A., M. Luca and C. Calandra (2013). "Sleep disorders and depression: brief review of the literature, case report, and nonpharmacologic interventions for depression." *Clin Interv Aging* **8**: 1033-1039.
- Mammen, G. and G. Faulkner (2013). "Physical activity and the prevention of depression: a systematic review of prospective studies." *Am J Prev Med* **45**(5): 649-657.
- Mitchell, A. J., M. Yadegarfar, J. Gill and B. Stubbs (2016). "Case finding and screening clinical utility of the Patient Health Questionnaire (PHQ-9 and PHQ-2) for depression in primary care: a diagnostic meta-analysis of 40 studies." *BJPsych Open* **2**(2): 127-138.
- Naci, H. and J. P. A. Ioannidis (2013). "Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study." *BMJ (Clinical Research Ed.)* **347**: f5577-f5577.
- O'Donoghue, G., C. Perchoux, K. Mensah, J. Lakerveld, H. van der Ploeg, C. Benaards, S. F. Chastin, C. Simon, D. O'Gorman and J. A. Nazare (2016). "A systematic review of correlates of sedentary behaviour in adults aged 18-65 years: a socio-ecological approach." *BMC Public Health* **16**: 163.
- Owen, N., G. N. Healy, C. E. Matthews and D. W. Dunstan (2010). "Too much sitting: the population health science of sedentary behavior." *Exerc Sport Sci Rev* **38**(3): 105-113.
- Pengpid, S., K. Peltzer, H. K. Kassean, J. P. Tsala Tsala, V. Sychareun and F. Muller-Riemenschneider (2015). "Physical inactivity and associated factors among university students in 23 low-, middle- and high-income countries." *Int J Public Health* **60**(5): 539-549.
- Prince, S. A., J. L. Reed, C. McFetridge, M. S. Tremblay and R. D. Reid (2017). "Correlates of sedentary behaviour in adults: a systematic review." *Obes Rev* **18**(8): 915-935.
- Rebar, A. L., R. Stanton and S. Rosenbaum (2017). "Comorbidity of depression and anxiety in exercise research." *Lancet Psychiatry* **4**(7): 519.
- Rock, P. L., J. P. Roiser, W. J. Riedel and A. D. Blackwell (2014). "Cognitive impairment in depression: a systematic review and meta-analysis." *Psychol Med* **44**(10): 2029-2040.
- Sallis, J. F., F. Bull, R. Guthold, G. W. Heath, S. Inoue, P. Kelly, A. L. Oyeyemi, L. G. Perez, J. Richards and P. C. Hallal (2016). "Progress in physical activity over the Olympic quadrennium." *Lancet*.
- Schuch, F., D. Vancampfort, J. Firth, S. Rosenbaum, P. Ward, T. Reichert, N. C. Bagatini, R. Bgeginski and B. Stubbs (2016). "Physical activity and sedentary behavior in people with major depressive disorder: A systematic review and meta-analysis." *J Affect Disord* **210**: 139-150.

- Schuch, F. B., D. Vancampfort, J. Richards, S. Rosenbaum, P. B. Ward and B. Stubbs (2016). "Exercise as a treatment for depression: A meta-analysis adjusting for publication bias." *J Psychiatr Res* **77**: 42-51.
- Sedentary Behaviour Research, N. (2012). "Letter to the Editor: Standardized use of the terms 'sedentary' and 'sedentary behaviours'." *Applied Physiology, Nutrition & Metabolism* **37**(3): 540-542.
- Soundy, A., C. Roskell, B. Stubbs and D. Vancampfort (2014). "Selection, use and psychometric properties of physical activity measures to assess individuals with severe mental illness: a narrative synthesis." *Archives Of Psychiatric Nursing* **28**(2): 135-151.
- Stanmore, E., B. Stubbs, D. Vancampfort, E. D. de Bruin and J. Firth (2017). "The effect of active video games on cognitive functioning in clinical and non-clinical populations: A meta-analysis of randomized controlled trials." *Neurosci Biobehav Rev* **78**: 34-43.
- Stubbs, B., T. T. Binnekade, A. Soundy, P. Schofield, I. P. J. Huijnen and L. H. P. Eggermont (2013). "Are Older Adults with Chronic Musculoskeletal Pain Less Active than Older Adults Without Pain? A Systematic Review and Meta-Analysis." *Pain Medicine* **14**(9): 1316-1331.
- Stubbs, B., J. Firth, A. Berry, F. B. Schuch, S. Rosenbaum, F. Gaughran, N. Veronesse, J. Williams, T. Craig, A. R. Yung and D. Vancampfort (2016). "How much physical activity do people with schizophrenia engage in? A systematic review, comparative meta-analysis and meta-regression." *Schizophr Res*.
- Stubbs, B., A. Koyanagi, M. Hallgren, J. Firth, J. Richards, F. Schuch, S. Rosenbaum, J. Mugisha, N. Veronese, J. Lahti and D. Vancampfort (2017). "Physical activity and anxiety: A perspective from the World Health Survey." *J Affect Disord* **208**: 545-552.
- Stubbs, B., A. Koyanagi, F. Schuch, J. Firth, S. Rosenbaum, F. Gaughran, J. Mugisha and D. Vancampfort (2016). "Physical Activity Levels and Psychosis: A Mediation Analysis of Factors Influencing Physical Activity Target Achievement Among 204 186 People Across 46 Low- and Middle-Income Countries." *Schizophrenia Bulletin*.
- Stubbs, B., A. Koyanagi, F. B. Schuch, J. Firth, S. Rosenbaum, N. Veronese, M. Solmi, J. Mugisha and D. Vancampfort (2016). "Physical activity and depression: a large cross-sectional, population-based study across 36 low- and middle-income countries." *Acta Psychiatr Scand* **134**(6): 546-556.
- Stubbs, B., A. Koyanagi, T. Thompson, N. Veronese, A. F. Carvalho, M. Solmi, J. Mugisha, P. Schofield, T. Cosco, N. Wilson and D. Vancampfort (2016). "The epidemiology of back pain and its relationship with depression, psychosis, anxiety, sleep disturbances, and stress sensitivity: Data from 43 low- and middle-income countries." *Gen Hosp Psychiatry* **43**: 63-70.
- Stubbs, B., S. Patchay, A. Soundy and P. Schofield (2014). "The Avoidance of Activities due to Fear of Falling Contributes to Sedentary Behavior among Community-Dwelling Older Adults with Chronic Musculoskeletal Pain: A Multisite Observational Study." *Pain Medicine (Malden, Mass.)*.
- Stubbs, B., D. Vancampfort, S. Rosenbaum, J. Firth, T. Cosco, N. Veronese, G. A. Salum and F. B. Schuch (2017). "An examination of the anxiolytic effects of exercise for people with anxiety and stress-related disorders: A meta-analysis." *Psychiatry Res* **249**: 102-108.
- Stubbs, B., D. Vancampfort, N. Veronese, K. G. Kahl, A. J. Mitchell, P. Y. Lin, P. T. Tseng, J. Mugisha, M. Solmi, A. F. Carvalho and A. Koyanagi (2017). "Depression and physical health multimorbidity: primary data and country-wide meta-analysis of population data from 190 593 people across 43 low- and middle-income countries." *Psychol Med*: 1-11.
- Stubbs, B., D. Vancampfort, N. Veronese, T. Thompson, M. Fornaro, P. Schofield, M. Solmi, J. Mugisha, A. F. Carvalho and A. Koyanagi (2017). "Depression and pain: primary data and meta-analysis among 237 952 people across 47 low- and middle-income countries." *Psychol Med*: 1-12.
- Tak, E., R. Kuiper, A. Chorus and M. Hopman-Rock (2013). "Prevention of onset and progression of basic ADL disability by physical activity in community dwelling older adults: A meta-analysis." *Ageing Research Reviews* **12**(1): 329-338.
- Teychenne, M., S. A. Costigan and K. Parker (2015). "The association between sedentary behaviour and risk of anxiety: a systematic review." *BMC Public Health* **15**: 513.

- Tremblay, M. S., S. Aubert, J. D. Barnes, T. J. Saunders, V. Carson, A. E. Latimer-Cheung, S. F. M. Chastin, T. M. Altenburg and M. J. M. Chinapaw (2017). "Sedentary Behavior Research Network (SBRN) - Terminology Consensus Project process and outcome." *Int J Behav Nutr Phys Act* **14**(1): 75.
- Vancampfort, D., C. U. Correll, B. Galling, M. Probst, M. De Hert, P. B. Ward, S. Rosenbaum, F. Gaughran, J. Lally and B. Stubbs (2016). "Diabetes mellitus in people with schizophrenia, bipolar disorder and major depressive disorder: a systematic review and large scale meta-analysis." *World Psychiatry* **15**(2): 166-174.
- Vancampfort, D., A. Koyanagi, M. Hallgren, M. Probst and B. Stubbs (2017). "The relationship between chronic physical conditions, multimorbidity and anxiety in the general population: A global perspective across 42 countries." *General Hospital Psychiatry* **45**: 1-6.
- Vancampfort, D., B. Stubbs, M. P. Herring, M. Hallgren and A. Koyanagi (2017). "Sedentary behavior and anxiety: Association and influential factors among 42,469 community-dwelling adults in six low- and middle-income countries." *Gen Hosp Psychiatry* **50**: 26-32.
- Vancampfort, D., B. Stubbs, A. J. Mitchell, M. De Hert, M. Wampers, P. B. Ward, S. Rosenbaum and C. U. Correll (2015). "Risk of metabolic syndrome and its components in people with schizophrenia and related psychotic disorders, bipolar disorder and major depressive disorder: a systematic review and meta-analysis." *World Psychiatry: Official Journal Of The World Psychiatric Association (WPA)* **14**(3): 339-347.
- Veronese, N., B. Stubbs, C. Trevisan, F. Bolzetta, M. De Rui, M. Solmi, L. Sartori, E. Musacchio, S. Zambon, E. Perissinotto, G. Baggio, G. Crepaldi, E. Manzato, S. Maggi and G. Sergi (2017). "Poor Physical Performance Predicts Future Onset of Depression in Elderly People: Pro.V.A. Longitudinal Study." *Phys Ther*.
- Ware, J., Jr., M. Kosinski and S. D. Keller (1996). "A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity." *Med Care* **34**(3): 220-233.
- Whiteford, H. A., A. J. Ferrari, L. Degenhardt, V. Feigin and T. Vos (2015). "The global burden of mental, neurological and substance use disorders: an analysis from the Global Burden of Disease Study 2010." *PLoS One* **10**(2): e0116820.
- Wirth, K., J. Klenk, S. Brefka, D. Dallmeier, K. Faehling, I. F. M. Roque, M. A. Tully, M. Gine-Garriga, P. Caserotti, A. Salva, D. Rothenbacher, M. Denking and B. Stubbs (2017). "Biomarkers associated with sedentary behaviour in older adults: A systematic review." *Ageing Res Rev* **35**: 87-111.
- Yamada, T., K. Hara, N. Shojima, T. Yamauchi and T. Kadowaki (2015). "Daytime Napping and the Risk of Cardiovascular Disease and All-Cause Mortality: A Prospective Study and Dose-Response Meta-Analysis." *Sleep* **38**(12): 1945-1953.
- Zamora-Macorra, M., E. F. de Castro, J. A. Avila-Funes, B. S. Manrique-Espinoza, R. Lopez-Ridaura, A. L. Sosa-Ortiz, P. L. Shields and D. S. Del Campo (2017). "The association between social support and cognitive function in Mexican adults aged 50 and older." *Arch Gerontol Geriatr* **68**: 113-118.
- Zhai, L., Y. Zhang and D. Zhang (2015). "Sedentary behaviour and the risk of depression: a meta-analysis." *Br J Sports Med* **49**(11): 705-709.

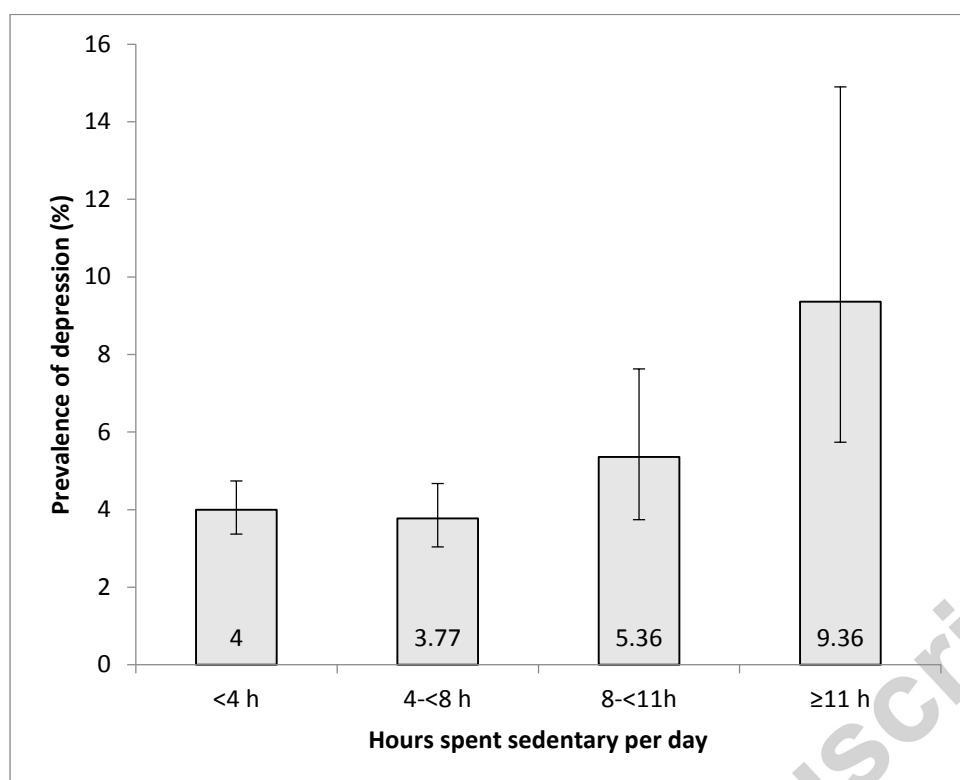


Figure 1 Prevalence of depression by hours of sedentary behavior per day

Estimates are based on weighted sample.

Bars denote 95% confidence intervals.

Table 1 Characteristics of the study sample

Characteristic		Unweighted N	Overall	Depression		P-value ^b	Highly sedentary behavior ^a		P-value ^b
				No	Yes		No	Yes	
Sex	Female	24,137	50.1	49.7	59.9	<0.001	50.1	50.6	0.853
Age (years)	18-49	8,340	72.7	73.3	59.5	<0.001	73.5	64.7	<0.001
	50-64	19,544	17.0	16.7	24.1		17.1	15.8	
	≥65	14,585	10.3	10.0	16.4		9.4	19.6	

			43.8	43.6	48.0	<0.0	43.6	46.6	0.02
	Mean (SD)		(14.4)	(14.3)	(16.7)	01	(14.0)	(17.7)	2
Wealth	Poorest	7,954	14.9	14.5	24.8	<0.0 01	15.1	13.2	0.09 9
	Poorer	8,292	17.8	17.6	24.2		18.0	16.3	
	Middle	8,259	18.8	18.7	20.4		18.7	21.4	
	Richer	8,758	21.1	21.4	14.4		21.7	15.9	
	Richest	9,026	27.3	27.8	16.2		26.6	33.2	
Education	≤Primary	25,451	43.1	42.2	63.1	<0.0 01	44.1	33.2	0.00 1
	Secondary	13,231	46.5	47.2	31.7		45.9	51.5	
	≥Tertiary	2,935	10.4	10.6	5.2		10.0	15.2	
Marital status	Married/co habiting	11,774	80.8	81.4	69.6	<0.0 01	82.0	72.1	<0.0 01
Setting	Rural	22,182	55.6	55.4	64.4	0.01 6	57.5	37.0	<0.0 01
Unemployed	Yes	23,778	38.5	37.9	51.6	<0.0 01	37.5	49.4	<0.0 01
Physical activity (min) ^c	Mean (SD)		1440 (1500)	1443 (1498)	1380 (1529)	0.46 4	1480 (1517)	1001 (1237)	<0.0 01
Alcohol consumption	Yes	7,805	21.9	22.3	9.7	<0.0 01	21.7	21.2	0.86 5
Smoking	Yes	11,275	35.2	35.0	39.2	0.13 0	34.9	36.6	0.61 7
Body mass index (kg/m ²)	Underweig ht	5,343	16.8	16.1	35.4	<0.0 01	17.3	13.3	0.00 5
	Normal	19,817	55.3	55.7	46.6		55.7	53.1	
	Overweigh t	9,625	20.9	21.2	13.5		20.5	22.9	
	Obese	5,229	7.0	7.0	4.6		6.6	10.7	

Social cohesion ^d	Mean (SD)		8.6 (4.9)	8.6 (4.8)	8.7 (6.0)	0.76 0	8.7 (4.9)	7.3 (4.3)	<0.0 01
Mobility ^e	Mean (SD)		18.0 (23.8)	16.8 (22.8)	46.5 (29.7)	<0.0 01	17.4 (23.1)	25.3 (29.0)	<0.0 01
Pain and discomfort ^e	Mean (SD)		19.6 (24.4)	18.4 (23.5)	47.8 (27.8)	<0.0 01	19.4 (24.1)	23.2 (26.9)	0.02 1
Cognition ^e	Mean (SD)		16.8 (23.6)	15.8 (22.7)	41.8 (30.9)	<0.0 01	16.7 (23.2)	19.6 (27.3)	0.05 6
Sleep and energy ^e	Mean (SD)		17.1 (23.4)	16.0 (22.3)	43.9 (31.4)	<0.0 01	16.4 (23.0)	24.4 (26.0)	<0.0 01
Vision ^e	Mean (SD)		14.6 (22.4)	13.9 (21.8)	31.3 (31.1)	<0.0 01	14.3 (22.0)	18.3 (25.6)	0.00 6
Anxiety	Yes	2,630	5.7	4.2	42.1	<0.0 01	5.6	7.6	0.03 7
Disability	Yes	2,440	3.1	2.5	18.0	<0.0 01	2.6	8.4	<0.0 01

Abbreviation: SD Standard deviation

Data are column percentage unless otherwise stated.

Estimates are based on weighted sample apart from the unweighted N.

^a Those spending ≥8 hours per day sedentary were considered to be highly sedentary.

^b The difference in sample characteristics by depression and sedentary behavior was tested by Chi-squared tests and Student's *t*-tests for categorical and continuous variables respectively.

^c The total amount of moderate-to-vigorous physical activity in a typical week.

^d Scores ranged from 9 to 45 with higher scores representing higher levels of social cohesion.

^e Scores ranged from 0 to 100 with higher scores representing worse health status.

Table 2 Association between depression and sedentary behavior assessed by multivariable logistic and linear regression (overall and by age groups)

	Logistic regression		Linear regression	
	Outcome (high SB ^a)		Outcome (min/day of SB)	
Sample	OR	95%CI	b-coefficient	95%CI

Overall ^b	1.94***	[1.31,2.85]	25.57**	[8.46,42.69]
Age 18-49 years ^b	2.19*	[1.06,4.52]	26.33*	[1.36,51.31]
Age 50-64 years ^b	1.66*	[1.11,2.49]	22.84*	[0.77,44.92]
Age ≥65 years ^b	1.72**	[1.21,2.45]	35.55**	[8.59,62.52]

Abbreviation: SB Sedentary behavior; OR Odds ratio; CI Confidence interval

^a Those reporting ≥8 hours per day spent sedentary were considered to be highly sedentary.

^b Adjusted for sex, age, wealth, education, marital status, setting, employment status, and country.

* p<0.05, ** p<0.01, *** p<0.001

Table 3 Health status, anxiety, and disability as mediators in the association between depression and highly sedentary behavior (overall and by age groups)

Mediator	Sample	Total effect	P-value	Direct effect	P-value	Indirect effect	P-value	% Mediated
Mobility	Overall	1.95 [1.32,2.89]	0.00 1	1.40 [0.94,2.09]	0.10 0	1.40 [1.25,1.56]	<0.0 01	49.9
	Age 18-49 years	2.20 [1.06,4.57]	0.03 4	1.64 [0.77,3.50]	0.20 0	1.34 [1.08,1.67]	0.00 8	37.2
	Age 50-64 years	1.65 [1.09,2.48]	0.01 7	1.29 [0.85,1.96]	0.22 5	1.27 [1.17,1.38]	<0.0 01	48.2
	Age ≥65 years	1.77 [1.23,2.55]	0.00 2	1.29 [0.91,1.84]	0.15 6	1.37 [1.23,1.53]	<0.0 01	55.2
Pain and discomfort	Overall	1.93 [1.32,2.83]	0.00 1	1.58 [1.07,2.32]	0.02 1	1.23 [1.12,1.34]	<0.0 01	31.1
	Age 18-49 years	2.18 [1.07,4.44]	0.03 2	1.88 [0.91,3.86]	0.08 7	1.16 [0.99,1.37]	0.07 5	NA
	Age 50-64 years	1.67 [1.11,2.52]	0.01 4	1.38 [0.92,2.07]	0.12 1	1.21 [1.12,1.31]	<0.0 01	37.3
	Age ≥65 years	1.75 [1.23,2.50]	0.00 2	1.30 [0.92,1.86]	0.14 0	1.34 [1.22,1.48]	<0.0 01	52.7
Cognition	Overall	1.93	0.00	1.73	0.00	1.11	0.00	16.1

		[1.30,2.85]	1	[1.16,2.59]	7	[1.03,1.20]	5	
	Age 18-49	2.20	0.03	2.43	0.02	0.90	0.28	NA
	years	[1.06,4.55]	4	[1.14,5.18]	2	[0.75,1.09]	1	
	Age 50-64	1.67	0.01	1.38	0.12	1.21	<0.0	37.0
	years	[1.11,2.52]	4	[0.92,2.09]	4	[1.12,1.30]	01	
	Age ≥65	1.75	0.00	1.48	0.03	1.18	<0.0	29.7
	years	[1.21,2.53]	3	[1.02,2.15]	8	[1.10,1.26]	01	
Sleep and energy	Overall	1.89	0.00	1.43	0.08	1.32	<0.0	43.4
		[1.27,2.82]	2	[0.95,2.17]	8	[1.17,1.48]	01	
	Age 18-49	2.11	0.05	1.53	0.28	1.38	0.00	42.8
	years	[0.99,4.49]	3	[0.70,3.34]	4	[1.13,1.68]	2	
	Age 50-64	1.66	0.01	1.35	0.15	1.23	<0.0	40.9
	years	[1.10,2.51]	5	[0.89,2.04]	4	[1.12,1.35]	01	
	Age ≥65	1.75	0.00	1.47	0.03	1.19	<0.0	30.5
	years	[1.22,2.50]	2	[1.02,2.13]	9	[1.10,1.28]	01	
Vision	Overall	1.91	0.00	1.78	0.00	1.07	0.00	11.0
		[1.29,2.82]	1	[1.21,2.62]	4	[1.02,1.13]	3	
	Age 18-49	2.14	0.03	2.02	0.05	1.06	0.18	NA
	years	[1.04,4.41]	9	[0.99,4.16]	5	[0.97,1.15]	0	
	Age 50-64	1.68	0.01	1.60	0.02	1.05	0.03	10.0
	years	[1.12,2.52]	2	[1.07,2.39]	3	[1.00,1.11]	3	
	Age ≥65	1.73	0.00	1.62	0.00	1.07	0.00	12.9
	years	[1.21,2.49]	3	[1.13,2.30]	8	[1.02,1.13]	5	
Anxiety	Overall	1.89	0.00	1.56	0.04	1.21	<0.0	30.0
		[1.26,2.83]	2	[1.01,2.42]	7	[1.08,1.35]	01	
	Age 18-49	2.17	0.04	1.95	0.10	1.11	0.34	NA
	years	[1.03,4.56]	2	[0.86,4.43]	9	[0.90,1.38]	1	
	Age 50-64	1.63	0.01	1.31	0.20	1.25	<0.0	45.4
	years	[1.08,2.45]	9	[0.86,1.97]	5	[1.11,1.41]	01	
	Age ≥65	1.71	0.00	1.42	0.06	1.20	<0.0	34.9

	years	[1.19,2.44]	4	[0.97,2.06]	8	[1.08,1.34]	01	
Disability	Overall	1.85	0.00	1.58	0.03	1.17	<0.0	25.6
		[1.23,2.78]	3	[1.04,2.39]	1	[1.10,1.25]	01	
	Age 18-49	2.12	0.05	1.81	0.13	1.17	0.01	20.5
	years	[0.99,4.50]	2	[0.83,3.94]	3	[1.04,1.31]	1	
	Age 50-64	1.64	0.01	1.53	0.04	1.07	0.00	14.5
	years	[1.09,2.47]	8	[1.00,2.32]	8	[1.02,1.13]	7	
	Age ≥65	1.68	0.00	1.37	0.09	1.22	<0.0	38.4
	years	[1.14,2.45]	8	[0.94,2.00]	7	[1.12,1.32]	01	

Data are odds ratio [95% confidence interval].

Models are adjusted for sex, age, wealth, education, marital status, setting, employment status, and country.

The mediated percentage was calculated only when the indirect effect was significant ($P < 0.05$).

Table 4 Physical activity, alcohol consumption, smoking, body mass index, and social cohesion as mediators in the association between depression and highly sedentary behavior

Mediator	Sample	Total effect	P-value	Direct effect	P-value	Indirect effect	P-value
Physical activity	Overall	1.98	0.001	1.93	0.001	1.03	0.649
		[1.33,2.95]		[1.30,2.87]		[0.99,1.07]	
	Age 18-49	2.23	0.033	2.20	0.036	1.02	0.512
	years	[1.07,4.68]		[1.05,4.59]		[0.97,1.07]	
	Age 50-64	1.66	0.016	1.63	0.020	1.02	0.311
	years	[1.10,2.51]		[1.08,2.47]		[0.98,1.05]	
	Age ≥65	1.77	0.003	1.71	0.006	1.04	0.212
	years	[1.22,2.55]		[1.17,2.50]		[0.98,1.10]	
Alcohol consumption	Overall	1.94	0.001	1.94	0.001	1.00	0.734
		[1.32,2.86]		[1.31,2.85]		[0.99,1.01]	
	Age 18-49	2.20	0.030	2.18	0.031	1.01	0.448
	years	[1.08,4.50]		[1.07,4.43]		[0.98,1.04]	
	Age 50-64	1.66	0.015	1.66	0.016	1.00	0.550

	years	[1.10,2.50]		[1.10,2.50]		[0.99,1.01]	
	Age ≥65	1.72		1.72		1.00	
			0.003		0.003		0.932
	years	[1.20,2.46]		[1.20,2.46]		[0.99,1.01]	
Smoking	Overall	1.93		1.91		1.01	
			0.001		0.001		0.276
		[1.31,2.84]		[1.30,2.81]		[0.99,1.03]	
	Age 18-49	2.18		2.18		1.00	
			0.033		0.033		0.910
	years	[1.06,4.46]		[1.07,4.47]		[0.97,1.03]	
	Age 50-64	1.66		1.66		1.00	
			0.015		0.015		0.491
	years	[1.11,2.50]		[1.10,2.49]		[0.99,1.01]	
	Age ≥65	1.73		1.71		1.01	
			0.003		0.003		0.201
	years	[1.21,2.47]		[1.19,2.45]		[0.99,1.03]	
Body mass index	Overall	1.97		1.97		1.00	
(kg/m ²)			0.001		0.001		0.901
		[1.31,2.96]		[1.31,2.96]		[0.99,1.02]	
	Age 18-49	2.23		2.26		0.99	
			0.028		0.026		0.472
	years	[1.09,4.58]		[1.10,4.64]		[0.96,1.02]	
	Age 50-64	1.63		1.61		1.01	
			0.031		0.037		0.494
	years	[1.05,2.54]		[1.03,2.54]		[0.98,1.04]	
	Age ≥65	1.76		1.78		0.99	
			0.004		0.004		0.328
	years	[1.19,2.59]		[1.21,2.62]		[0.97,1.01]	
Social cohesion	Overall	1.92		1.91		1.00	
			0.001		0.001		0.782
		[1.30,2.83]		[1.29,2.82]		[0.98,1.03]	
	Age 18-49	2.17		2.17		1.00	
			0.037		0.037		0.997
	years	[1.05,4.48]		[1.05,4.48]		[0.98,1.02]	
	Age 50-64	1.65		1.63		1.01	
			0.018		0.021		0.361
	years	[1.09,2.50]		[1.08,2.46]		[0.98,1.04]	
	Age ≥65	1.73		1.70		1.02	
			0.002		0.003		0.315
	years	[1.22,2.45]		[1.20,2.41]		[0.98,1.06]	

Data are odds ratio [95% confidence interval].

Models are adjusted for sex, age, wealth, education, marital status, setting, employment status, and country.

The mediated percentage was not calculated as the indirect effect was not significant for any of the mediators.

Highlights

- This is the first multinational study investigating the association between sedentary behaviour and depression.
- People with depression spent 25.6 (95%CI 8.5-42.7) more minutes per day in SB than non-depressed participants.
- The relationship between SB and depression was most notable in older people.
- Factors influencing the SB and depression relationship included mobility limitations (49.9%), followed by impairments in sleep/energy (43.4%), pain/discomfort (31.1%), anxiety (30.0%), disability (25.6%).